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International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 4 : C07D 401/12, A61K 31/415 — A1

(11) International Publication Number: WO 88/ 03921

(43) International Publication Date: 2 June 1988 (02.06.88)

(21) International Application Number: PCT/SE87/00546

(22) International Filing Date: 20 November 1987 (20.11.87)

(31) Priority Application Numbers: 8604998-8, 8605551-4, 8704049-9

(32) Priority Dates: 21 November 1986 (21.11.86), 23 December 1986 (23.12.86), 16 October 1987 (16.10.87)

(33) Priority Country: SE

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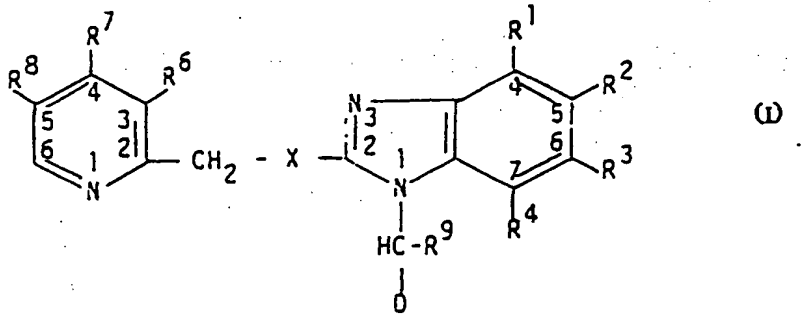
(81) Designated States: AT, AT (European patent), AU, BB, BE (European patent), BG, BJ (OAPI patent), BR, CF (OAPI patent), CG (OAPI patent), CH, CH (European patent), CM (OAPI patent), DE, DE (European patent), DK, FI, FR (European patent), GA (OAPI patent), GB, GB (European patent), HU, IT (European patent), JP, KP, KR, LK, LU, LU (European patent), MC, MG, ML (OAPI patent), MR (OAPI patent), MW, NL, NL (European patent), NO, RO, SD, SE, SE (European patent), SN (OAPI patent), SU, TD (OAPI patent), TG (OAPI patent), US.

Published
With international search report.

(54) Title: NEW BENZIMIDAZOLE DERIVATIVES A PROCESS FOR PRODUCTION THEREOF AND A PHARMACEUTICAL COMPOSITION CONTAINING THE SAME



(I)

(57) Abstract

Novel compounds of formula (I), pharmaceutical compositions containing such compounds as active ingredient, and the use of the compounds in medicine.

Examples I 21 and I 22

1-chloromethyl-(5-methoxy) and (6-methoxy)-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl) methyl]sulfinyl]-1H-benzimidazole.

1-hydroxy methyl-(5-methoxy)and-(6-methoxy)-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl) methyl]sulfinyl]- 1H-benzimidazole (30 g 0.08 mol ratio 1:2) was dissolved in toluene (500 ml) and the solution was cooled to -30°C. A solution of thionyl chloride (19 g 0.16 mol) in toluene (100 ml) was added dropwise at -30°C and the mixture was stirred for 10 minutes at -30°C. Then a solution of triethyl amine (45 g 0.45 mol) in toluene (200 ml) was added dropwise. After the addition the temperature was raised and the mixture stirred at room temperature for 30 minutes. The mixture was evaporated and the residue (120 g) was chromatographed on silica gel (ethylacetate-methylenechloride 50-50) giving the title compound as an isomeric mixture (ratio 1:3) Yield 11.9 g.

NMR (500 MHz, $CDCl_3$) 2.23, 2.25, 2.26, 3.72, 3.87, 3.92, 4.88, 4.95, 4.96, 6.17, 6.18, 6.54, 6.57, 6.95, 7.01, 7.19, 7.26, 7.43, 7.67, 8.17.
If desired the pure 1-chloromethyl 6-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole was obtained when the isomeric mixture was crystallized in acetonitrile.
NMR (500 MHz, $CDCl_3$) 2.23, 2.25, 3.72, 3.92, 4.88, 4.96, 6.17, 6.57, 6.95, 7.01, 7.67, 8.17.

Preparation of Phosphoric acid, cyanoethyl-[6-methoxy-[2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole-1-yl]]methyl diester, triethylammonium salt (Method B)

1-Chloromethyl-6-methoxy-2[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole (0.90 g, 0.0023 mol) was added under stirring to a solution of mono-triethylammonium salt of phosphoric acid cyanoethyl ester (0.70 g, 0.0028 mol) and triethyl amine (0.65 g, 0.0064 mol)